The management of spinal metastasis in children

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Objective: To seek an optimal treatment plan from the results of treatment for metastatic disease of the spine in children.

Design: An 8-year retrospective study of children with metastatic disease of the spine. Imaging studies were reviewed and treatment modalities analysed.

Setting: The divisions of pediatric orthopedics and pediatric neurosurgery at the Children's Hospital of Eastern Ontario, Ottawa.

Patients: All children seen between April 1980 and December 1987 who had lesions metastatic to the spine by hematogenous or direct extension. There were 20 children (15 boys, 5 girls) with a mean age at the time of diagnosis of 9.5 years. Follow-up ranged from 2 weeks to 108 months. One child was lost to follow-up.

Interventions: Eleven children underwent laminectomy and decompression. Of the 14 neurologically compromised children, 5 received chemotherapy and radiotherapy and 9 received chemotherapy, radiotherapy and surgery.

Main outcome measures: Type of metastatic lesion, vertebrae involved and response to therapy.

Results: Vertebrae involved with metastases were as follows: cervical (3), thoracic (5), lumbar (8) and multilevel (2). Meninges were involved in 2 cases. The most common causes of metastatic spinal involvement were neuroblastoma (4 cases) and astrocytoma (6 cases). Pathologic fractures occurred in 4 children and kyphoscoliosis in 4. Spinal cord paresis developed in 14 of the 20 children. Of the 6 children who survived from 48 to 108 months, 5 had tumours of neural origin, 4 being astrocytomas. Children with neuroblastoma or leukemic infiltration had a good initial response to chemotherapy. Five of the 6 surviving children had astrocytomas, and 5 were treated by surgical decompression.

Conclusions: Metastatic disease of the spine in children secondary to astrocytoma should be treated aggressively, but from the experience gained from this study it is impossible to devise a rigid treatment plan for each type of metastatic tumour. The choice of chemotherapy, radiotherapy or surgery depends on the type of tumour, the age of the child and whether or not the spinal cord is compromised.

Objectif : Chercher un plan de traitement optimal à partir des résultats du traitement de métastases à la colonne chez les enfants.

Conception : Étude rétrospective d'une durée de 8 ans portant sur des enfants atteints de métastases à la colonne. On a examiné des études d'imagerie et analysé les modes de traitement.

Contexte : Les divisions d'orthopédie pédiatrique et de neurochirurgie pédiatrique à l'Hôpital pour enfants de l'est de l'Ontario, à Ottawa.

Patients : Tous les enfants examinés entre avril 1980 et décembre 1987 qui avaient des métastases à la colonne produites par dissémination hématogène ou directe. Les 20 enfants (15 garçons, 5 filles) avaient en moyenne 9,5 ans au moment du diagnostic. La durée du suivi a varié de deux semaines à 108 mois. Un enfant a été perdu au suivi.

Interventions : Onze enfants ont subi une laminectomie et une décompression. Sur les 14 enfants at-

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teints neurologiquement, 5 ont été traités par chimiothérapie et radiothérapie et 9, par chimiothérapie, radiothérapie et chirurgie.

PRINCIPALES MESURES DES RÉSULTATS : Type de lésion métastatique, vertèbre atteinte et réaction au traitement.

RÉSULTATS : Les métastases avaient atteint les vertèbres suivantes : cervicales (3), thoraciques (5), lombaires (8) et multiples (2). Les méninges étaient atteintes dans deux cas. Les métastases à la colonne étaient causées le plus souvent par un neuroblastome (4 cas) et un astrocytome (6 cas). Quatre enfants ont subi des fractures pathologiques et quatre autres ont été atteints d'une cyphoscoliose. Une parésie de la moelle épinière a fait son apparition chez 14 des 20 enfants. Sur les 6 enfants qui ont survécu de 48 à 108 mois, 5 avaient des tumeurs d'origine neurologique, des astrocytomes dans quatre cas. Les enfants atteints d'un neuroblastome ou d'une infiltration leucémique ont bien réagi au début à la chimiothérapie. Cinq des six enfants survivants avaient un astrocytome et cinq ont été traités par décompression chirurgicale.

CONCLUSIONS : Les métastases à la colonne causées par un astrocytome devraient être traitées de façon agressive chez les enfants, mais d'après l'expérience tirée de cette étude, il est impossible de concevoir un plan de traitement rigide pour chaque type de tumeur métastatique. Le choix de la chimiothérapie, de la radiothérapie ou de la chirurgie dépend du type de tumeur, de l'âge de l'enfant et de l'atteinte de la moelle épinière.

Bone is the third most frequent site for distant metastases of lung and liver tumours respectively. Within the skeletal system, the vertebral column is most commonly involved.[1] In adults who succumb to cancer, 70% have been shown to have spinal metastases.[2–5] With improved chemotherapeutic regimens, radiation techniques and surgical advances children with malignant disease of the spine are surviving longer.[2] Direct extension of spinal cord tumours into the vertebral column is the second major mechanism of tumour encroachment into the spine. To date, there have been limited studies on vertebral metastases in children. We reviewed our experience with children who had metastatic spinal disease and cord involvement to better understand the natural history of the disease and to use the results to recommend methods for improving survival and quality of life.

PATIENTS AND METHODS

All 20 children treated for metastatic disease of the spine at the Children's Hospital of Eastern Ontario between April 1980 and December 1987 were studied. Six of them were alive at the time we conducted this study. We analysed the hospital records, radiotherapy and chemotherapy records of all patients (Table I).

There were 5 girls and 15 boys. The mean age at the time of diagnosis and treatment was 9.5 years (range from 1 day to 16 years). The mean follow-up for the 6 living patients was 72 months (range from 48 to 108 months). The 12 children who died had a mean follow-up of 20 months (range from 2 weeks to 66 months). One child was followed up for 24 months before the family moved out of the province. One child was lost to follow-up soon after discharge from hospital.

RESULTS

Presenting signs and symptoms

Although pain was the most common presenting symptom in this series, a change in gait pattern was the most common presenting sign. In 6 children, radicular pain developed followed by progressive weakness, sensory loss, anal and urethral sphincter dysfunction and irreversible paraplegia. Pathological fractures occurred in 4 children, resulting in considerable morbidity (Fig. 1). Significant spinal deformity was also encountered in 4 children, 2 with progressive kyphosis (Fig. 2) and 2 with scoliosis.

Diagnosis

Several diagnostic techniques were used to detect metastatic lesions. Plain radiographs were used to identify osteogenic or sclerotic lesions. Technetium-99m bone scanning was used to detect osteoblastic activity (Fig. 3). Open vertebral biopsy in 10 children was 100% successful in obtaining a pathological diagnosis. MRI was found to be the most useful of all the diagnostic methods used (Fig. 4, right).

The diagnoses in these 20 children were as follows: neuroblastoma (4), astrocytoma (6), acute lymphocytic leukemia (2) , schwannoma (2), Ewing sarcoma (1) (Fig. 5), medulloblastoma (1), osteosarcoma (1), meningeal sarcoma (1), primitive neuroectodermal tumour (1) and optic glioma (1).

The cervical spine was involved in 3 patients, the thoracic spine in 6 and the lumbar spine in 7; there was multilevel involvement in 2 and meningeal involvement in 2. The types of tumours found in the 6 survivors are described in Table II.

Treatment

The treatment and outcome in the 20 children in this study are shown in Table I. Radiotherapy (30 to 40 Gy) was used to treat radiosensitive tumours, especially in cases of neurologic impairment and in young children. If radiotherapy

failed to relieve spinal cord compression, surgery was carried out. Collapsed vertebral bodies in 2 children were replaced by bone grafts. Fourteen children received chemotherapy alone (3) or in combination with radiotherapy (4) or surgery (2) or both (5). Four children underwent surgery alone, 1 child re-

Table I

Characteristics of 20 Children Who Had Spinal Metastasis

Patient no.	Sex/age, yr	Diagnosis	Level	Treatment	Follow-up, mo	Outcome
1	M/17	Ewing sarcoma	Lumbar	Chemotherapy	66, until death	Progressive neurologic deterioration, paraplegia, widespread metastasis
2	M/10	Medulloblastoma	Multilevel	Chemotherapy, radiotherapy	3, until death	Brief improvement of neurologic function
3	M/1 d	Neuroblastoma	Lumbar	Chemotherapy	18, until death	Significant neurologic improvement. Staphylococcal septicemia
4	M/5 wk	Neuroblastoma	Lumbar	Chemotherapy, surgery	24, moved away	Increasing motor function, diminished sphincter control
5	M/6	Neuroblastoma	Lumbar	Chemotherapy	2 wk, until death	Widespread metastasis
6	F/4	Neuroblastoma	Lumbar	Chemotherapy, radiotherapy	7, until death	Back pain, neurologic bladder, widespread metastasis
7	M/1 d	Astrocytoma	Cervical	Laminectomy	52	Increased activity in lower limbs, ankle clonus on dorsiflexion. Doing well
8	M/15	Osteogenic sarcoma	Lumbar	Chemotherapy, surgery	5, until death	Pulmonary metastasis
9	M/6	Meningeal sarcoma	Meninges	Radiotherapy	Lost	—
10	M/15	Schwannoma	Thoracic	Chemotherapy, radiotherapy	24, until death	Paraplegia, superior vena caval syndrome
11	M/11	Primitive neuroectodermal tumour	Thoracic	Chemotherapy, radiotherapy, surgery	36, until death	From paraplegia could stand, take steps, pain controlled, symptom free, then multilevel involvement
12	M/15	Astrocytoma	Thoracic	Radiotherapy, laminectomy	48	No recurrence, doing well, left leg weakness
13	M/17	Astrocytoma	Cervical	Laminectomy	72	Brown–Séquard syndrome deficit reversed, some deficit C7 dermatome
14	F/15	Astrocytoma	Thoracic	Chemotherapy, radiotherapy, surgery	9, until death	Horner syndrome, hemiparesis, downhill course
15	F/16	Schannoma	Thoracic	Chemotherapy, radiotherapy, surgery	2, until death	Less pain
16	F/8 mo	Astrocytoma	Cervical	Surgery	7, until death	Head tilt to right improved
17	M/14	Acute lymphocytic leukemia	Multilevel	Chemotherapy, radiotherapy, bone-marrow transplant	60	Pain free, last follow-up March 1987 and PRN
18	M/3	Acute lymphocytic leukemia	Meninges	Chemotherapy, radiotherapy	66, until death	Neurologic improvement, cerebral metastasis
19	F/17	Optic glioma	Lumbar	Chemotherapy, radiotherapy, surgery	108	Estrogen replacement needed, doing well
20	M/6	Astrocytoma	Thoracic	Laminectomy	65	No pain, bilateral lower limb weakness

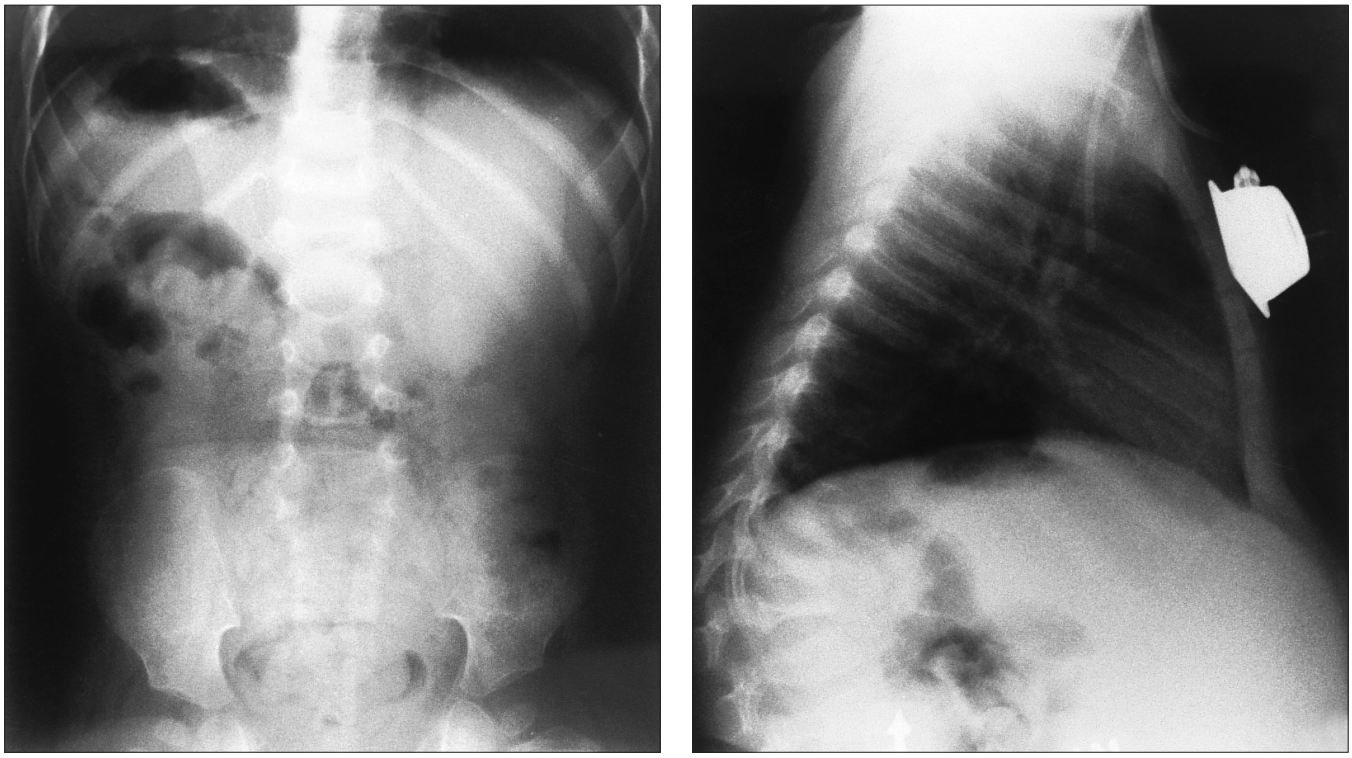

FIG. 1. Patient 3 (Table I). There is a compression fracture of the T12 and L1 vertebral bodies secondary to metastatic neuroblastoma.

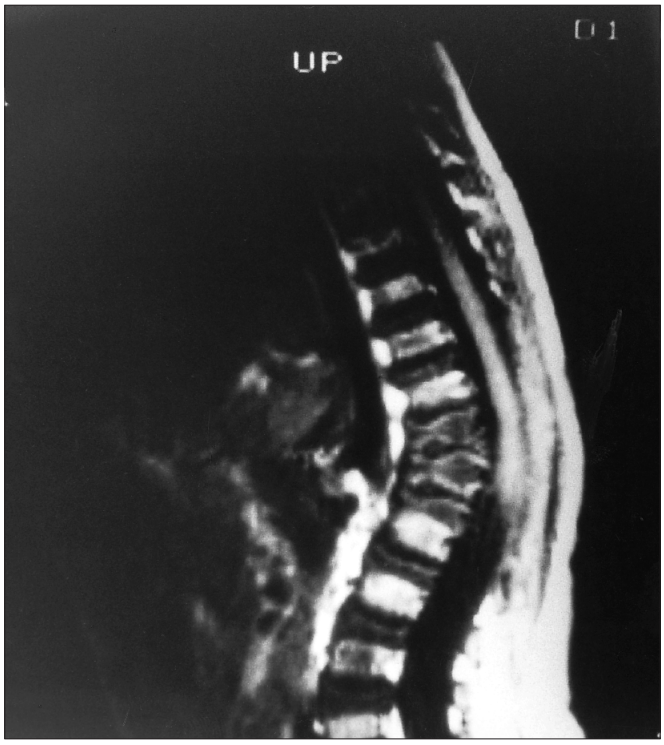

FIG. 2. Patient 3. MRI illustrating kyphotic deformity secondary to vertebral body collapse from metastatic neuroblastoma at T12 and L1.

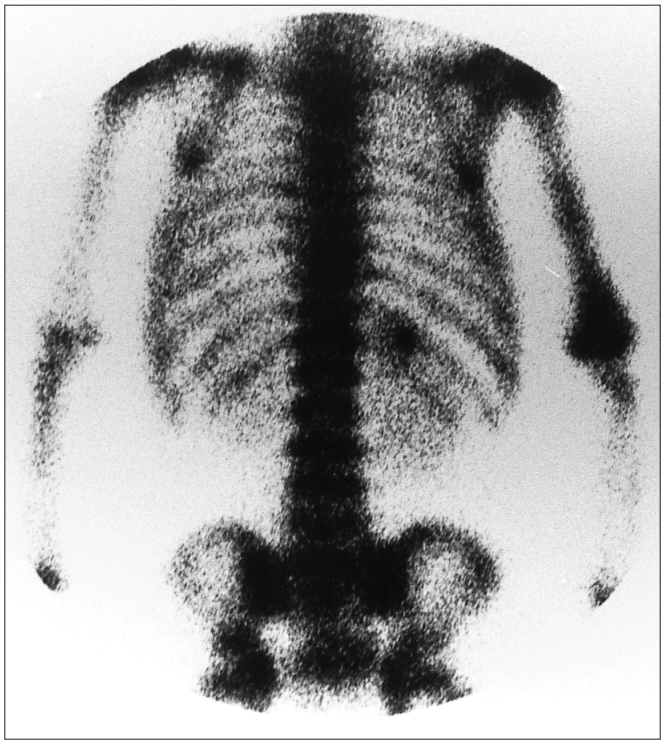

FIG. 3. Patient 6. A technetium-99m bone scan shows numerous metastatic bone lesions secondary to neuroblastoma.

ceived radiotherapy alone and 1 had surgery and radiotherapy. Of the 6 children who were still alive at the completion of the study, 5 had laminectomy with resection of tumour and 1 was treated by chemotherapy and radiation (Table II). We experienced a good response initially to chemotherapy in children with leukemic infiltration or neuroblastoma.

Neural tumours

Of the 20 tumours studied in this review, 12 were from metastases or direct extension from a tumour of neural origin. Of the 6 surviving children, 5 had tumours of neural origin, 4 of these being astrocytomas. Metastatic disease of the spine secondary to astrocytoma therefore

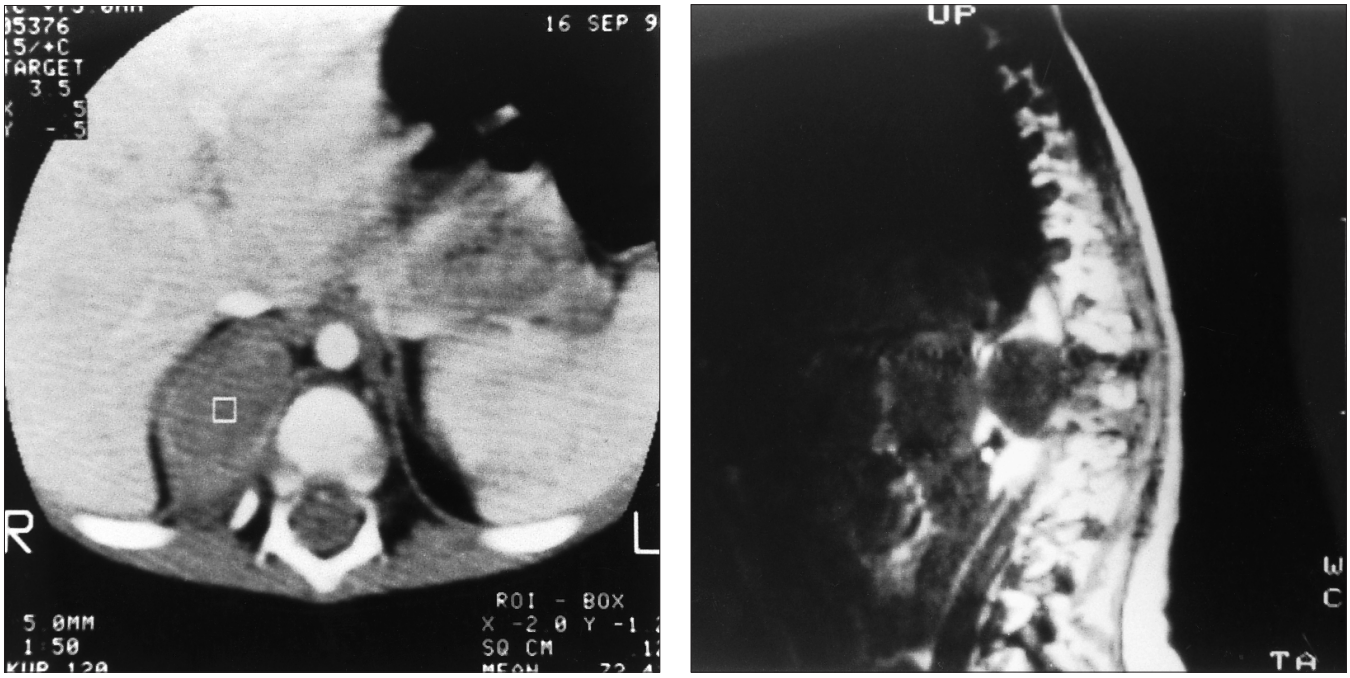

FIG. 4. Patient 3. (A) CT scan. An axial cut through the neuroblastoma reveals a metastatic lesion in T12. (B) MRI illustrates the extent of the tumour much better, including the entire extent of spinal involvement.

Table II

Characteristics of 6 Surviving Children Who Had Spinal Metastasis

Patient no.	Diagnosis	Level	Treatment	Follow-up
7	Astrocytoma	Cervical	Vertebrectomy T4, T5 Decompression C7–T4 Laminectomy and fusion	52 mo, bilateral paraparesis, increased spontaneous activity of lower limbs
12	Astrocytoma	Thoracic	Laminectomy T8–10 with subtotal excision of tumour. Radiotherapy	48 mo, weakness of left leg
13	Astrocytoma	Cervical	Laminectomy C2–7, biopsy 2nd stage, radical removal of tumour, intraoperative urodynamics plus fusion. Chemotherapy and radiotherapy	72 mo, deficit C7 dermatome
17	Acute lymphocytic leukemia	Cervical	Radiotherapy and bone-marrow transplant	120 mo, pain free
19	Optic glioma	Lumbar	Resection of glioma and laminectomy L5–S1, postop radiotherapy, bilateral ventriculoperitoneal shunt	108 mo, needs estrogen replacement
20	Astrocytoma	Thoracic	Laminectomy T7–10 and fusion	65 mo, no pain, lower limb weakness bilaterally

should be particularly aggressively treated since the longevity and success of treatment appear to exceed those of other metastatic tumours.

Non-neural tumours

The success rate of treatment for non-neural tumours, of which there were 8 in this review, was not high in terms of longevity. Only 1 child with acute lymphocytic leukemia was alive at the time this review was completed. This may be related to the fact that metastases to other organs have occurred by the time the vertebral metastases have been identified.

Spinal cord involvement

Fourteen children had spinal cord involvement. Eight were ambulatory with minor weakness of the lower limbs resulting in a limp, 1 was ambulatory with L3 cauda equina syndrome and 1 was ambulatory with thoracomyelopathy and polyradiculopathy. Thoracolumbar cord paraparesis developed in 6 children, cervical cord paraparesis in 2 children, lower extremity hemiparesis with Horner syndrome in 1 child and Brown–Séquard syndrome associated with numbness in the left hand in 1 child.

Discussion

Metastatic disease to the spine in children is uncommon and often not well documented. Very few studies have addressed this problem in children. Although many primary tumours may metastasize to the axial skeleton, neuroblastoma and astrocytoma appear to be most common in the pediatric age group (Table I).

There are three pathophysiologic mechanisms for metastasis to the spine: the tumour mass may extend directly from its primary paravertebral region; it may migrate via the lymphatic vessels into the intervertebral foramen; or it may hematogenously deposit in the bone marrow by way of venous plexus.[6] According to Harrington[4] and Boland, Lane and Sundaresan,[3] interconnecting channels of the valveless vertebral veins communicate with intercostal and lumbar veins, thus allowing deposition of tumour cells during increased intra-abdominal pressure. Symptoms arise due to spinal cord or nerve root compression, compounded by vascular congestion, hemorrhage and edema but often without penetration of the dura,[2–4] as in 14 of the children in this study. Spinal structural deformities such as kyphosis and scoliosis secondary to osteolytic changes with pathological fractures of the vertebral body may also occur; they were demonstrated in 4 children in this study.[3–5] Although the lumbar spine was the most commonly affected, cord compression was more frequently encountered in the thoracic region due to its high cord-to-canal diameter ratio.[3,4] Several children had radicular pain, progressive weakness, sensory loss, anal or urethral sphincter dysfunction and irreversible paraplegia. Early neurologic symptoms as a result of cord or spinal root compression occurred without plain radiographic detection of metastatic lesions in 2 of our patients. Generally, if fulminant neurologic sequelae developed within 24 hours of the onset of initial symptoms, the prognosis was very poor.[3,4]

Several diagnostic techniques were employed to identify the metastatic lesions. Plain radiographs were used for osteogenic or sclerotic lesions. However, these changes may be difficult to

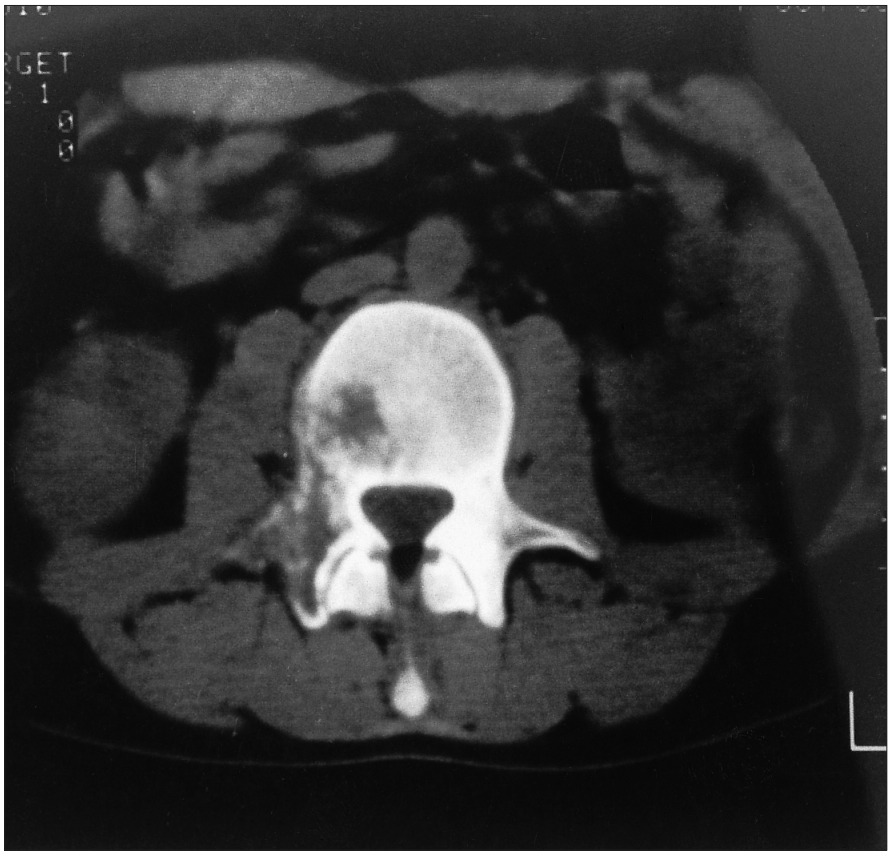

FIG. 5. Patient 1. A CT scan shows metastatic Ewing sarcoma to L3.

differentiate from osteoporosis initially.[3,4] For a plain film to unequivocally demonstrate vertebral body infiltration, 30% to 50% bony destruction must take place.[3,4] If, however, the pedicle is absent, the "winking owl sign" is clear evidence of pedicle erosion and an early indication of cortical bone invasion[7] caused by tumour necrosis.[2]

We found the technetium-99m bone scan useful because of its ability to detect osteoblastic activity (Fig. 3),[8] recognizing that hot spots are also present in arthritis, infections and traumatic fractures.[3,4] Depending on whether the procedure is percutaneous or open, vertebral biopsy is diagnostic in 65% and 85% of cases respectively.[3,4]

We found the most useful method in identifying metastatic lesions was MRI. In contrast to the CT scan, which is limited to a transaxial plane, the MRI is able to scan the entire spine sagittally and coronally (Fig. 4).[8] Although metrizamide myelography will demonstrate a partial or total block localizing the site of cord compression, it is nevertheless an invasive procedure with possible side effects from the injection of contrast material (Fig. 6).[8] Other major advantages of MRI include superior resolution without the use of ionizing radiation or contrast material.[8] All children with metastatic spine disease should undergo MRI of the spinal column to delineate the extent of the lesion in both the vertebrae and spinal canal.

In pediatric patients with new or impending paralysis from metastatic or locally invasive cancer, the current initial treatment recommended is chemotherapy, spinal radiation and possibly intravenous administration of steroids. It has been suggested that in the absence of extensive neurologic involvement or vertebral collapse or instability, chemotherapy should be used exclusively in the treatment of spinal metastases.[3,4] Some investigators have clearly demonstrated the effectiveness of a multiagent regimen of chemotherapy, which includes a combination of cyclophosphamide, vincristine, cisplatin, VM-26 and doxorubicin,[9] for the management of cord compression due to metastatic disease from childhood neuroblastoma.[9–11] Sanderson, Pritchard and Marsh[9] reported full restoration of neurologic function including normal sphincter function and a 15% to 20% long-term survival rate when chemotherapy was used as the initial treatment. Similarly, Pritchard and colleagues[12] showed that 22% of the children with bony metastasis from neuroblastoma survived a median of 61 months when only chemotherapy was administered. The concomitant use of high-dose corticosteroid, dexamethasone, may also be a major contributor in pain relief.[1,9] We experienced a similar initial good response with chemotherapy in children with leukemia infiltration or neuroblastoma. In general, chemotherapy was used most frequently in children with neuroblastoma and in very young children. Surgical decompression was effective in older children and in children with tumours that are less responsive to chemotherapy such as astrocytoma (Table I).

Radiotherapy was used in radiosensitive tumours especially if there was evidence of neurologic impairment but no significant compromise of the integrity of the bony vertebral structures.[3,4] Surgical intervention was pursued if irradiation failed to provide adequate relief of spinal cord compression and there was still severe pain with further neurologic deficit or the appearance of kyphosis.[3,4,13,14] We believe that surgical decompression should be considered when the metastatic tumour has destroyed enough bone to result in progressive deformity with mechanical pain or fragments of bone or disc compressing the spinal cord directly.

The decision to perform anterior or posterior decompression was determined by the anatomic location and the mechanical disorder caused by the tumour. MRI was extremely helpful in making this decision. The advantages of an "anterior approach" include the ability to resect an anteriorly located tumour as well as the correction of kyphotic deformities.[3,4] The collapsed vertebral bodies in cases of kyphosis repair may be replaced by

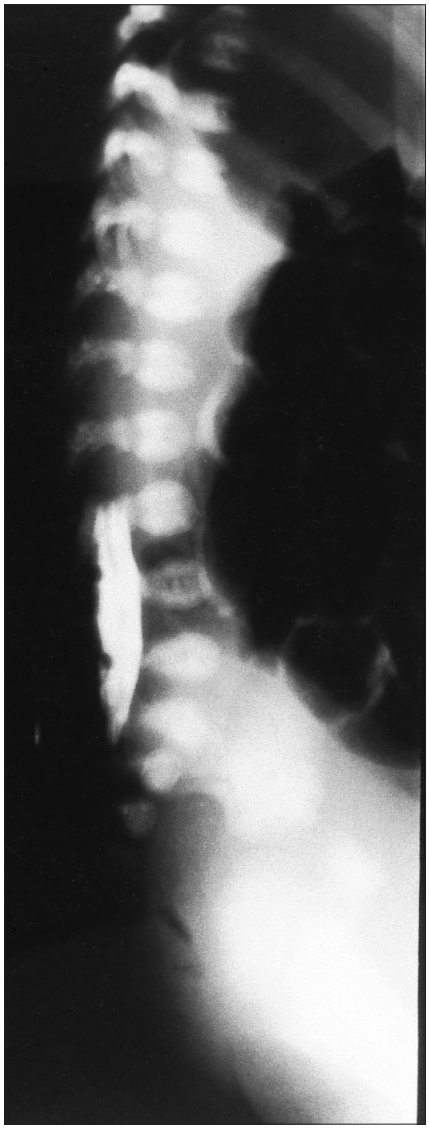

FIG. 6. Patient 4. A metastatic neuroblastoma causing a complete block of the canal at L3–4 with paraplegia syndrome.

constructs fused with metallic struts. The results of anterior compression in the literature have been satisfactory, with pain relief in 90% of the patients, compared with 80% in those who underwent a "posterior" laminectomy.[7] Disadvantages of the anterior approach include the inability to decompress the spinal cord circumferentially and dependence on the patients' ability to withstand a trans-thoracic and transabdominal procedure.[7,15,16]

The posterior laminectomy approach, on the other hand, is suitable for a multilevel vertebral decompression in the region of the lamina or pedicle.[3,4] However, the removal of posterior bony elements along with the stripping of supportive ligamentous structures necessitates stabilization with fixation devices such as Luque rods.[7] Postoperative management of such children is facilitated by the use of an aliplast soft Boston orthosis (Fig. 7).

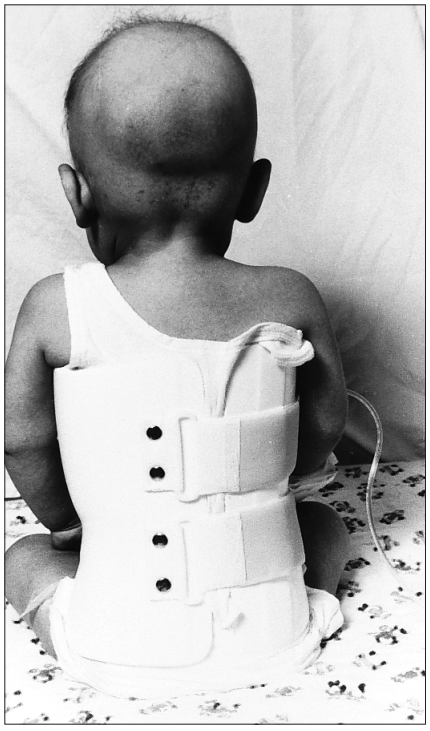

FIG. 7. Patient 3 is shown in a soft Boston aliplast prosthesis, which allowed comfortable upright sitting in the presence of vertebral metastasis.

We have found that this type of orthosis is well tolerated by young children with back pain who are undergoing chemotherapy or radiotherapy.[17]

Post-surgical spinal deformity has been reported in 49% of children who underwent epidural tumour excision and laminectomy.[14] According to Lonstein,[14] kyphosis is a result of bone loss as well as the loss of ligaments such as supraspinous ligament, interspinous ligament, ligamentum flavum and joint capsule of facets, which all contribute to the stability of the spinal column in the prevention of anterior collapse.

In view of our experience, it appears that although surgery often provides significant pain relief and effective spinal cord and nerve root decompression, spinal stabilization is required to prevent progressive kyphosis.[18,19] It is interesting that of our 6 surviving children, 5 were treated by surgical decompression (Table II). Surgery, chemotherapy and radiotherapy all contribute to the effective management of the pediatric cancer patient with vertebral metastases. The indications and contraindications, advantages and disadvantages of each of the 3 modalities of treatment must be carefully considered in order to devise an effective treatment plan for spinal metastases in children. The factors governing the development of an effective therapeutic strategy for complicated metastatic disease of the spine in children cannot be rigidly mandated. The choice of one or more modalities of treatment depends on the type of tumour, the age of the child and whether the spinal cord is compromised.

Conclusions

Metastatic disease of the spine in children is associated with a high death rate. Metastatic tumours of the spine of neural origin, especially astrocytomas, have a better prognosis. Surgical decompression of the spinal cord secondary to metastatic tumours will help to improve and preserve neurologic function. Spinal fusion after posterior laminectomy prevents late spinal deformity. The choice of chemotherapy, radiotherapy or surgery depends on the type of tumour, the age of the child and whether or not the spinal cord is compromised; a rigid treatment plan cannot be devised for each type of metastatic tumour.

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Notices
Avis

BiOS Europe '97

A joint meeting of the European Laser Association (ELA) and the International Biomedical Optics Society (IBOS) will be held at the Hotel Londra/Centro Congressi, Sanremo, Italy, from Sept. 4 to 8, 1997. For further information contact: Direct Communications GmbH, Attn. Ms. Karin Burger, Xantener Str. 22, D-10707 Berlin, FR Germany. Tel.: 49 30 881 50 47; fax: 49 30 88 68 29 46; e-mail:100140.3211@compuserve.com

Congress on biomedical peer review

The *Journal of the American Medical Association*, the *British Medical Journal* and Project HOPE announce The International Congress on Biomedical Peer Review and Global Communication to be held in Prague, Czech Republic, from Sept. 17 to 21, 1997. For further information contact: Annette Flanagin, *JAMA*, 515 N State, Chicago IL 60610, USA. Tel.: 312 464-2432; fax: 312 464-5824; e-mail: aff@ix.netcom.com

The pediatric esophagus

The Department of Pediatric Surgery, Faculty of Medicine, Ege University, Izmir, Turkey, will host an interdisciplinary symposium entitled "The pediatric esophagus" from Apr. 20 to 22, 1998, in Izmir (URL—http://medicine.ege.edu.tr/pedsurg/ped_oesophagus.htm). The main topic will be gastroesophageal reflux with a special interest in alkaline reflux. For further information contact: Professor Oktay Mutaf, Department of Pediatric Surgery, Ege University Faculty of Medicine, 35100 Izmir, Turkey. Fax: +90 (232) 3 75 12 88; e-mail: mutaf@bornova.ege.edu.tr

International Federation of Societies for Surgery of the Hand

"The future at hand: sharing knowledge towards the 21st century" will be the theme of the 7th Congress of the International Federation of Societies for Surgery of the Hand (IFSSH). The congress, hosted by the IFSSH and MANUS Canada will be held from May 24 to 28, 1998, at the Vancouver Trade and Convention Centre, Vancouver, BC. For further information contact: Conference Secretariat — Events by Design, 601–325 Howe St., Vancouver BC V6C 1Z7. Tel.: 604 669-7175; fax: 604 669-7083; e-mail: 74117.273@compuserve.com■